Potential utility of providing high-intensity, variable step training for improving locomotion in patients across neurological disorders

T. George Hornby, PT, PhD
Associate Professor
Department of Physical Therapy and Kinesiology & Nutrition
University of Illinois at Chicago

Director, Locomotor Recovery Laboratory
Director of Research, Ability Lab
Rehabilitation Institute of Chicago

Strategies to improve locomotor function in patients with neurological injury

- Functional Electrical Stimulation
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- Resistance training/therapeutic exercise
- Body-weight supported treadmill training
- Robotic-assisted training
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- Resistance training/therapeutic exercise
- Body-weight supported treadmill training
- Robotic-assisted training
- Alternative therapies
  - Hydrotherapy
  - Tai Chi
  - Acupuncture

Attempts to apply “principles of neuroplasticity” to locomotor training interventions

- Animal/human studies have identified specific factors that influence neuroplasticity (Kleim and Jones 2008)
  1. Use it or lose it*
  2. Use it and improve it*
  3. Specificity Matters
  4. Repetition Matters
  5. Intensity Matters
  6. Time Matters
  7. Salience Matters
  8. Age Matters
  9. Transference
  10. Interference
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Current clinical practice
- Lacks high dosages of stepping practice (average 100-800 steps/session during in- and out-patient rehabilitation; Lang et al 2009)
- Lacks cardiovascular intensity (2.8 mins/session spent in heart rate zone)

Important parameters of rehabilitation interventions

- **Amount** of specific practice are important intervention parameters (Hesse 1995, Pohl 2002, Sullivan 2007, Moore 2010)
  - Task-specific practice is thought to mediate activity-dependent neuroplasticity (Edgerton 2012, Liepert 1998)
  - Animal studies suggest thousands of repetitions are necessary for neuroplastic changes (DeLeon 1999)
How does “amount of practice” contribute to locomotor outcomes?

- Individuals post-stroke do not receive substantial amounts of task-specific practice during rehabilitation (Lang et al 2007, 2009)

- Could higher doses of stepping result in improved walking ability? (Moore et al 2010)

Dose-response relationships: Moore et al 2010

- Large amounts of stepping practice post-stroke (Moore et al 2010)
  - Monitored stepping activity with Step Activity Monitors (SAMs)
  - Stepping during regular PT ~200-1000 steps/session
  - Stepping during locomotor training ~2000-6000 steps/session
Dose-response relationships:
Moore et al 2010

- **Dose** = stepping practice during therapy/training
- **Response** = improvements in daily stepping following therapy/training

### Important parameters of rehabilitation interventions

- **Intensity** is also important
  - Training at higher speeds/cardiovascular intensities (Holleran 2014, Macko 2005) demonstrate greater improvements in locomotor function
    - Increased NGF/BDNF, enhanced muscular oxidative capacity
    - Increased cardiorespiratory function, decreased submaximal exertion
  - Motl and Pilutti 2012 Nature Rev Neurol

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**Dose**
- A stepping practice during PT/IT

**Response**
- Δ daily stepping post-PT/IT

Relation between stepping practice and change in daily stepping:

- Stroke
- Motl and Pilutti 2012 Nature Rev Neurol

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**Power (watts)**

- **Maximal oxygen uptake (L/min)**

**Endurance**

- **Conditioned**, **Normal**, **Sedentary**
Comparison of high- vs low-intensity stepping

- Robotic vs therapist-assisted training post-stroke
  - Robotic-assisted – guided, symmetrical stepping
  - Therapist-assisted – assist-as-needed

- Patients with chronic hemiparesis, (Hornby et al 2008)
  - Training – 12 30-min sessions
  - Testing – Post and 6 month follow-up

- Similar amount of practice

Therapist vs Robotic Assisted Training in Chronic Stroke

- Doubled improvements with therapist vs robotic assistance
- Consistent across severity of walking impairments
- May be due to differences in cardiovascular responses during training (Israel et al 2006, Hornby et al 2012)
Additional finding about errors during stepping training?

- Lokomat entrained symmetrical gait pattern
- Those who received robotic-assisted training demonstrated less symmetry

![Graph showing % single limb stance and Step length asymmetry](image)

Contribution of errors and variability of locomotor practice??

- Just walking on a treadmill at high intensity doesn’t always elicit gains in walking function (Macko et al 2005, Moore et al 2010)
- Augmenting errors during learning may enhance magnitude/accelerate learning (Bastian 2006, Reisman et al 2010)
- Greater errors associated with variable contexts
  - Task/environmental variability
    - Shah et al 2012 - Forward vs variable treadmill training
    - van den Brand et al 2012 - Forward treadmill vs Overground/stairs
- Is variability important? What should be variable? How much? When?
Outline

- Introduction
  - Contribution of amount and “intensity” of task-specific locomotor practice
  - Many studies minimize potential contributions of errors and variability

- Feasibility of providing large amounts of stepping activity in variable contexts in subacute/chronic stroke
  - Effects on locomotor behaviors
  - Effects on non-locomotor behaviors

- Future directions and clinical application

Preliminary feasibility study

- Given 1 hr, how much locomotor practice can we provide?
  - Maximize stepping practice? At high intensity?
  - Variable contexts/environments with sufficient challenge?
    - What is sufficient challenge - how hard?
    - What should patients have to adapt to during locomotor interventions?

- If only “higher level” locomotor training is practiced, can “lower level” tasks improve?
  - Leap-frog hypothesis (Horn et al 2005)
  - Reverse transfer (vs Gentile’s Taxonomy)
Pilot study - Methods

• Subjects: 22/25 individuals post-stroke completed ≥ 4 weeks
  – Unilateral hemiparesis, requires moderate assistance to ambulatory but < 0.9 m/s self-selected walking speed
  – 10 w/chronic stroke (> 6 mo; all ambulatory, duration = 41.2 mo)
  – 12 w/ subacute stroke (1-6 mo, 3 non-ambulatory, duration = 3.2 mo)

• 3 subjects terminated:
  – Relocation
  – Intolerance to exercise
  – Previously unreported medical issue (pulsatile mass in neck)

Methods

• Testing:
  – 1 month prior to training (chronic)
  – BSL, Post-4, Post-8, 3 month follow-up

• Locomotor outcomes:
  – Stepping activity during/outside of training
  – Self-selected, fastest possible 10 m, 6 min walk
  – Gait kinematics/symmetry
  – Peak VO2, gait efficiency and economy

• Non-locomotor outcomes
  – 5X sit-to-stand (time/kinematics/kinetics)
  – Berg Balance Scale
Methods: Training duration/amount

- Up to 40 1-hr sessions over 8-10 weeks

- Protocol: focus on directional stepping
  - First 2 weeks – all treadmill training (focus on speed/intensity)
  - Weeks 3-8:
    - Half treadmill: 25% speed training, 25% dynamic balance
    - Half overground: 25% speed/balance, 25% stairs
    - Monitoring stepping activity, HR/RPE throughout

- Priorities of training
  - Focus only on stepping
  - High aerobic intensity (70-80% heart rate reserve, up to 18 RPE)
  - Variability - Intensity/challenge enhanced with successful completion, switching between tasks

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Increasing challenge/difficulty

Walking is continuous task, biomechanical subcomponents can be challenged separately
Challenging biomechanical subcomponents of walking

- Weight bearing/propulsion
  - Guidance/Assist-as needed – weight support, slow speeds
  - Error Augmentation –
    - Reduce weight support/assist as tolerated
    - Increase speed, propulsive demands/add weighted vest

- Leg swing
  - Guidance/Assist-as needed – manual/elastic assistance
  - Error Augmentation – elastic resistance, leg weights, stepping over obstacles

- Medial-lateral/anterior-posterior stability
  - Guidance/Assist-as needed – stabilize trunk, assistive devices
  - Error Augmentation – balance perturbations

“Worst case” scenario

Baseline testing
“Best case” scenario

Primary locomotor outcomes

- Daily and training stepping activity
  - Per day prior to, during and following training (post and follow-up)
  - Stepping activity during training (ave = 2873 per session – note: just treadmill is ~4000 steps/session)
Primary locomotor outcomes

• Gait velocity:
  – SSV: chronic = 0.23 m/s; subacute = 0.33 m/s (Effect size -1.34-1.64)
  – FV: chronic = 0.38 m/s; subacute = 0.54 m/s (ES: 1.53-1.62)
  – Recent published changes= 0.18 m/s (Ada et al 2003; different inclusion), subacute ~0.25 m/s (LEAPS)

Primary locomotor outcomes

• Six minute walk test:
  – chronic = 90 m; Ada et al 2003 ~60 m
  – subacute = 144 m; recent ~80 m (LEAPS)
• Approx. 33-50% reduction in O₂ cost (ES: 0.62-1.08)
Primary locomotor outcomes

• Relationship between stepping dosage vs outcomes (6 min walk)

• No relation between initial impairments and change

![Graph showing stepping dosage vs 6 min walk outcomes]

B: initial vs Δ6 min walk

y = 0.01x + 117
r = 0.00

Initial 6 min walk (m)

Secondary locomotor outcomes

• Gait symmetry
  – Single leg paretic limb stance time improvement from 20 to 26% (normal 40%; ES 1.35-1.68)
  – Step length asymmetry: 8 to 15% improvement (p = 0.06, ES = 0.50-0.84)

• Graded treadmill tests
  – Peak velocity increased from 0.5-6 to 0.9-1.0 m/s
  – Peak VO₂ increased by ~19%, efficiency improved by 13%
  – Kinetic/kinematic data
    • Increased active ROM for hip, knee, ankle sagittal plane
    • Increase moment/power generation for all
    • Primary determinants of gait speed are changes in non-paretic limb

![Graph showing graded treadmill tests results]
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Secondary non-locomotor outcomes

- Five times sit-to-stand decrease
  - 25% chronic,
  - 40% subacute

- Berg Balance Scale
  - 6 pts chronic,
  - 8 pts subacute (~21 pts non-ambulatory)
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Preliminary data: Single-blinded RCT in subacute stroke
Application to other diagnoses

• Do the same principles translate to other neurological populations?
  – Why wouldn’t they?
  – What are the potential concerns?

• Specifics related to multiple sclerosis
  – Increased fatigue???
  – Increased spasticity/uncoordinated movement???
  – Increased community participation/quality of life???

Conclusions

▪ Rationale for providing large amounts of high intensity, variable stepping activities

▪ Providing such interventions is feasible
  ▪ Effects on locomotor behaviors
  ▪ Effects on non-locomotor behaviors

▪ Future directions and clinical application
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Thank you and Questions?
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